## REMARKS/ARGUMENTS

Claims 1 to 18 have been canceled without prejudice and applicant reserves the right to pursue the subject matter of these claims at a latter date. New claims 19 to 50 have been added to more clearly present the invention. No new matter has been added.

The Examiner rejects the pending claims under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make or use the invention. Specifically, the Examiner states that the claims encompass making transgenic avians and clones and that the only purpose of the methods is to obtain a germline chick that carries the exogenous nucleic acid in its germ cells and passes the nucleic acid on to its offspring. The Examiner also states that merely transferring exogenous nucleic acid into a recipient embryo does not have an enabled use without obtaining a germline chimera. Applicant traverses this rejection.

Applicant submits that introduction of nucleic acids into an avian embryo is useful for purposes beyond those described by the Examiner. For example, introducing nucleic acids into avian embryos as disclosed in the present specification is useful for research purposes including those described in the Examples of the specification.

However, applicant includes data herein which demonstrates that the invention, as disclosed in the present specification, is useful to produce transgenic avians (Table A).

Until the present invention researchers working on avian embryo micromanipulation have relied on the use of stereo or upright microscopes combined with a micromanipulator to inject the embryo (Love, J, *et al.* Biotechnology (N Y) 12: 60-3, 1994 and Naito, M, *et al.* Mol Reprod Dev 37: 167-71, 1994). In these systems, the objective is located above the injection micropipette or needle and the surface of the egg. These systems have provided mixed results. One factor likely a contributor to these mixed results is that these systems severely limit the imaging of the injection site since the micropipette or needle is positioned in front of the injection site in which case the operator cannot visualize whether the micropipette is indeed inside the germinal disk or to know the depth of the micropipette within the ooplasm. In the present invention, among other things, the capability to visualize the micropipette relative to the embryo is provided.

The present invention employs a system which allows the operator to visualize how deep the injection pipette is inserted inside the egg's ooplasm (see Figure A). This new feature is of great value. For example, without wishing to limit the invention to any particular mechanism or theory of operation, it is believed that a procedure which introduces DNA into the embryo, and is minimally disruptive to the embryo, will provide the embryo an opportunity to develop normally and produce a chick. For example, inserting the micropipette too deeply into the embryo may cause loss of viability of the embryo. Conversely, if the micropipette tip does not penetrate the embryo, the nucleic

acid will not enter the embryo. This invention represents a microinjection system that can precisely and reliably deliver nucleic acids into avian embryos

**Figure A**

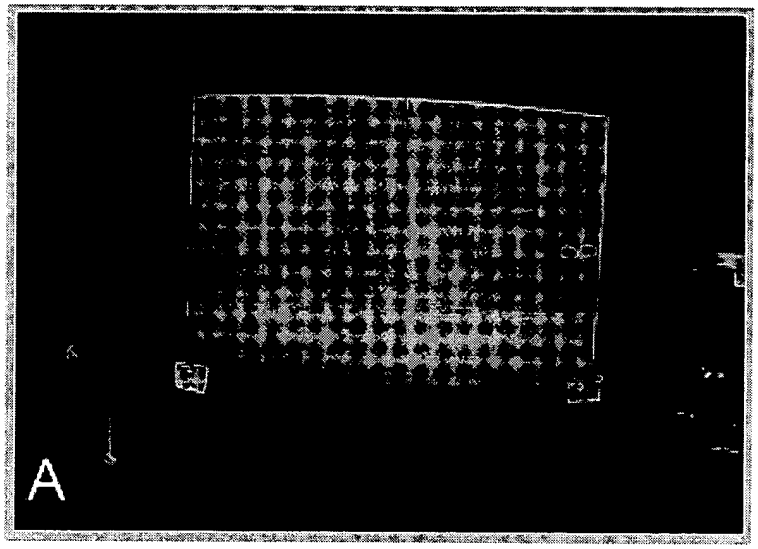


Figure A shows an image of a micropipette tip of the present invention on the surface of a chicken embryo.

**Table A**

| Protein | Construct | DNA Config. | Blood (DNA) Positive/Tested | Semen (DNA) Positive/Tested | Egg White (Protein) Positive/Tested |
|---|---|---|---|---|---|
| Recombinant Protein 1 | 70 kb OM-IRES-1 | Linear | 1/103 | 4/48 | 17/55 |
| Recombinant Protein 2 | CMV-2<br>RSV-2 | Linear<br>Linear | 5/51<br>32/132 | 1/23<br>9/62 | 0/28<br>11/70 |
| Recombinant Protein 3 | 10 kb OM-3<br>12 kb-Lys-3 | Linear<br>Linear | 1/29<br>2/119 | 6/14<br>6/51 | 0/10<br>3/41 |
| | | | | | |

Table A shows the production of three different proteins, using various constructs and promoters, in eggs of transgenic chickens produced in accordance with the present invention. Chickens positive/tested for the nucleic acid (blood and semen) and encoded protein (egg white) produced by embryo microinjection are shown.

In conclusion, applicant has shown that the present claims meet the requirements for patentability under the 35 USC 112, first paragraph, enablement provision. Therefore, applicant submits that the presently pending claims are allowable and respectfully requests the Examiner to pass the above-identified application to allowance.

If any issues remain unresolved, or if the Examiner has any questions, it is requested that the Examiner call applicant's attorney at the number below.

Respectfully submitted,

Kyle Yesland, 706-227-1170 ext. 233
Attorney for Applicants
Reg. No. 45,526
AviGenics, Inc.
Legal Department
111 Riverbend Road
Athens, Georgia 30605